PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WPP290109	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/GB2004/050033	International filing date *(day/month/year)* 02.12.2004	Priority date *(day/month/year)* 02.12.2003
International Patent Classification (IPC) or national classification and IPC C07D307/60, C07D307/62, A61K31/365, A61P25/00, A61P29/00, A61P35/00		
Applicant NEUROPHARMA, S.A. et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.09.2005	14.02.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Hanisch, I Telephone No. +49 89 2399-7880

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/050033

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-15 as originally filed

   Claims, Numbers

   1-16 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 15,16 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. 15,16 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/050033

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	2,4,7-10,12,14
	No:	Claims	1,3,5,6,11,13,15,16
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III.

Claims 15 and 16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

Relevant prior art is provided by

(A) J. Nat. Prod. 2002, 65, 1307-1314
(B) J. Nat. Prod. 2001, 64, 1301-1304
(C) J. Nat. Prod. 1998, 51, 275-281
(D) J. Org. Chem. 1999, 64, 9258-9260
(E) Chem. Pharm. Bull. 1997, 45(1), 181-184
(F) WO 0185685

Novelty

None of (A)-(F) disclose the use of compounds falling within the scope of current formulae I or II (claims 1 or 7) as claimed in the current claims. Consequently, the requirements of Article 33(2) PCT appear to be fulfilled.

Inventive Step

The problem underlying the present application appears to be the provision of further compounds which are useful for the treatment of GSK-3 mediated diseases such as i.a. cancer or inflammation. (A) could be considered to be the closest prior art since it discloses compounds which fall within the current general formula and have been reported to show cytotoxicity against human tumor cell lines. No mechanism is provided. In this respect, however, it should be noted that although a discovery of a mechanism a chemical entity triggers in the body (such as inhibiting GSK-3) may be an important piece of scientific knowledge, it cannot be considered as a technical contribution to the art. It is only the therapeutic effect of a medicament, namely treating specific diseases, which is relevant for the assessment of inventive step; In the current case this means e.g. the treatment of cancer or inflammation.

Consequently, prior art documents relating to e.g. anticancer agents such as (A)-(C) belong to the current technical field. Taking into account the furanosesterterpenes known from (A)-(E) the skilled person would by way of a generalization of these compounds have arrived at the present compounds of formula I. Since there was, moreover, a clear indication in the prior art that these compounds are active against human tumor cell lines (e.g. in (A)) as well as against inflammation (see e.g. (D)) the skilled person would automatically check their usefulness as anticancer and anti-inflammatory agents in pharmaceutical preparations. An inventive step in the sense of Article 33(3) PCT may therefore only be acknowledged for claims 1, 11, 15 and 16 if the compounds of formula I have a surprising improved effect vis-à-vis the closest state of the art. Such an effect, however, remains to be elucidated.
However, no indication prompted the skilled person to arrive at the subgroup of formula II. An inventive step may therefore be acknowledged for these compounds (claim 7) and their use (claim 2).

Industrial Applicability

For the assessment of the present claims 15 and 16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.